IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of:			
Barkur G. BHAT *et al.*		Art Unit:	1631
Appln. No.:	09/267,199	Examiner:	Marjorie A. Moran
Filed:	March 12, 1999	Atty. Docket:	16517.233
For:	Nucleic Acid Molecules and Other Molecules Associated with the Tocopherol Pathway	Confirmation No.	6701

APPELLANT'S BRIEF

Mail Stop Appeal Brief – Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

This is an Appeal from the Final Rejection of all claims pending in the above-captioned patent application. A Notice of Appeal was filed on September 16, 2003. Authorization to charge the official fees for this filing is given in the accompanying transmittal letter. *This Brief is submitted in triplicate.*

1. Real Party in Interest

The real party in interest is Monsanto Company, a Delaware corporation with offices at 800 North Lindbergh Boulevard, St. Louis, Missouri 63167.

2. Related Appeals and Interferences

Appellant is unaware of any Appeals or Interferences related to this Appeal.

3. Status of Claims

Claims 10-18, 20-22, and 25 are pending. Claims 10-18, 20-22, and 25 stand finally rejected under 35 U.S.C. §§ 101 and 112, first paragraph. Appellant appeals all of the rejections of claims 10-18, 20-22, and 25.

4. Status of Amendments

Appellant has not filed any responses subsequent to Final Rejection in this case.

5. Summary of Invention

The invention is directed to a nucleic acid molecule comprising a sequence that hybridizes under conditions of 2.0 X sodium chloride/sodium citrate (SSC) at about 65°C to a nucleic acid molecule having a sequence selected from the group consisting of SEQ ID NOs: 100, 147, 153, 180, 199, 232 and complements thereof. Specification at page 23, lines 4-8 and at page 60, line 16 through page 61, line 10. The invention is also directed to a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 1, 100, 147, 153, 158, 161, 180, 184, 199, 232 and complements thereof. Specification at page 23, line 4 to page 26, line 17. The invention is also directed to a nucleic acid molecule consisting of a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 1, 100, 147, 153, 158, 161, 180, 184, 199, 232 and complements thereof. *Id.* The invention is also directed to a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1 or complement thereof. Specification at page 23, lines 4-18. The invention is also directed to a nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO: 158 or complement thereof. Specification at page 24, line 22 to page 25, line 14. The invention is also directed to a nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO: 161 or complement thereof. Specification at page 25, lines 15-23.

6. Issues

The issues in this Appeal are:

(a) whether claims 10-18, 20-22, and 25 are unpatentable under 35 U.S.C. § 101 for allegedly being unsupported by a specific asserted utility or a well established utility;

(b) whether claims 10-18, 20-22, and 25 are unpatentable under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement because the claimed invention purportedly lacks utility; and

(c) whether claims 10-18 and 20-22 are unpatentable under 35 U.S.C. § 112, first paragraph, for alleged insufficiency of written description.

7. Grouping of Claims

Independent claims 10-18, 20-22, and 25 remain in this case. Claims 10, 12, 16, 17, 22 and 25 are independent. All of the claims at issue do not stand or fall together. The separate patentability of claims 10-18, 20-22 and 25 is addressed in Sections 8.A through 8.C below. The separate patentability of claims 10-18 and 20-22 is addressed in Section 8.D below. A copy of the claims on appeal is attached hereto as Appendix A.

8. Argument

A. Summary of Appellant's Position

As the Supreme Court said in *Brenner v. Manson*, the "basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility....where specific benefit exists in currently available form." 383 U.S. 519, 534-35, 148 U.S.P.Q. 689, 695 (1966). Applicants have met their part of the bargain – they have disclosed nucleic acid molecules which, in their current form, provide at least one specific benefit to the public, for example use to identify the presence or absence of a polymorphism in a population of maize or soybean plants. This benefit is specific, not vague or unknown, and it is a "real world" or substantial benefit. Because the claimed nucleic acid molecules provide at

least these benefits, they satisfy the utility requirement of 35 U.S.C. § 101. Because the specification teaches how to make and use the claimed nucleic acid molecules for the disclosed utilities, the enablement requirement of 35 U.S.C. § 112 has been met.

Furthermore, Applicants have provided an adequate description of the claimed nucleic acid molecules that demonstrates Applicants' possession of the claimed invention of claims 10-18 and 20-22. The genera of claimed nucleic acid molecules, *e.g.*, the genus of nucleic acid molecules comprising the nucleic acid sequences of SEQ ID NOs: 100, 147, 153, 180, 199 and 232 of claim 10, for example, have been described by the recitation of common structural features, *e.g.*, the nucleotide sequences of SEQ ID NO s: 100, 147, 153, 180, 199 and 232, which distinguishes molecules in the claimed genera from molecules not in the claimed genera.[1] Because the specification demonstrates that Applicants had possession of (and have provided an adequate description of) the claimed genera of nucleic acid molecules, the specification satisfies the written description requirement of 35 U.S.C. § 112.

B. The Claimed Nucleic Acids Have Legal Utility

Claims 10-18, 20-22 and 25 stand rejected under 35 U.S.C. § 101 as allegedly not supported by a "specific, substantial, and credible utility or by a well established utility." Final Action mailed June 17, 2003 (Paper No. 27) ("Final Action"), at page 2.

The rejection is based upon two basic premises. First, the Examiner asserts that the asserted uses "are general uses (purposes) applicable to the general class of nucleic acids and are not specific" to the claimed sequences. *Id.* Second, the Examiner argues that the specification does not show that the claimed sequences actually encode an

[1] This assertion applies with equal force to all of the nucleic acid molecules of the present invention, including, for example, nucleic acid molecules comprising the nucleic acid sequences of SEQ ID NOs: 158 and 184 as in claim 22, and nucleic acid molecules comprising the nucleic acid sequence of SEQ ID NO: 1 as in claim 12.

enzyme of the tocopherol pathway, the open reading frames of the encoded peptides or start and stop codons. *Id.* at 3.

This analysis misstates the nature of the asserted uses, ignores disclosed utilities, and misapplies the doctrine of "practical utility" developed by the courts after *Brenner v. Manson*. The "threshold for utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip, Inc. v. Orange Bang, Inc.*, 185 F.3d 1364, 1366, 51 U.S.P.Q.2d 1700, 1702 (Fed. Cir. 1999), *citing Brenner v. Manson*, 383 U.S. 519, 534 (1966). Furthermore, an invention need only provide one identifiable benefit to satisfy 35 U.S.C. § 101. *See Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983) ("when a properly claimed invention meets at least one stated objective, utility under section 101 is clearly shown").

The courts have expressed a test for utility that hinges on whether an invention provides an "identifiable benefit." *Juicy Whip*, 185 F.3d at 1366, 51 USPQ.2d at 1702. For analytical purposes, the requirement for an "identifiable benefit" may be broken into two prongs: (1) the invention must have a specific, *i.e.*, not vague or unknown benefit, *In re Brana*, 51 F.3d 1560, 1565, 34 U.S.P.Q.2d 1436, 1440 (Fed. Cir. 1995); and (2) the invention must provide a real world, *i.e.*, practical or "substantial" benefit. *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1563, 39 U.S.P.Q.2d 1895, 1899 (Fed. Cir. 1996). A corollary to this test for utility is that the invention must not be "totally incapable of achieving a useful result," *i.e.*, the utility must not be incredible or unbelievable. *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 U.S.P.Q.2d 1401, 1412 (Fed. Cir. 1992).

Applicants have asserted in the specification that the claimed nucleic acid molecules provide identifiable benefits, for example, use to identify the presence or absence of a polymorphism, use as a hybridization probe for expression profiling, and use to modulate tocopherol enzyme levels in plant cells. *See, e.g.*, specification at page 84 line 18 through page 92, line 11, page 97, line 22 to page 98, line 18 and page 128, line

17 to page 132, line 10. Any of these utilities described alone is enough to satisfy Section 101. Because Applicants need only establish a single utility to satisfy 35 U.S.C. § 101, and have done so in the present case, the premise of the rejection under Section 101 is incorrect, and the rejection should be reversed.

(1) The Claimed Nucleic Acid Molecules Provide A Specific Benefit, *i.e.*, They Have Specific Utility

The Examiner acknowledges that the specification describes multiple utilities for the present invention, including "probes for assisting in the isolation of full-length cDNAs or genes which would be used to make protein and optionally further usage to make the corresponding antibodies, gene mapping, isolation of homologous sequences, detection of gene expression such as in Northern blot analysis, molecular weight markers, chromosomal markers, and for numerous other generic genetic engineering usages." Office Action mailed November 21, 2000 (Paper Number 7), at page 5. Furthermore, the Examiner acknowledges that it is well known in the art that polynucleotides "can be used in hybridization assays to obtain other (e.g. homologous or complementary) nucleic acid sequences, to identify polymorphisms, etc." Final Office Action at page 2. Moreover, the specification also discloses additional utilities for the claimed nucleic acid molecules,[2] including introduction of the claimed nucleic acid molecules into a plant or plant cell (either as sense or antisense inhibitors), which can then be used to screen for phenotypic variations in tocopherol levels and synthesis in a variety of plants. Specification at page 11, lines 12-23 and at page 128, line 6 through page 131, line 9. For example, a compound can be provided to both an antisense plant and a control plant (no antisense) and the effect of the compound on the plant can be monitored. Such a screen is analogous to a cell-based assay, which has a legally sufficient utility.[3] Other

[2] It is irrelevant whether the corresponding mRNA or polypeptide have utility because Applicants are not relying on utility of the mRNA or polypeptide to establish utility of the claimed nucleic acid molecules.

[3] *See, e.g.*, MPEP § 2107 at page 2100-32.

utilities disclosed in the specification include use of the claimed nucleic acid molecules to measure the level of mRNA in a sample,[4] and use as molecular markers.[5]

(a) Identifying the Presence or Absence of a Polymorphism

More particularly, one of the utilities disclosed in the specification is use of the claimed nucleic acid molecules to identify the presence or absence of a polymorphism. Specification at page 84, line 18 through page 92, line 11. The Examiner argues that this utility, like many of the asserted utilities, is not specific to the claimed sequences, Final Office Action at page 2, but does not provide any support (legal or factual) for the proposition that detection of polymorphisms using the claimed nucleic acid molecules is not a legal utility.

Many of the disclosed utilities in this case, including the detection of polymorphisms, are directly analogous to the utilities of a microscope, *i.e.*, the claimed nucleic acid molecules may be used to locate and measure nucleic acid molecules within a sample, cell, or organism. The fact that, *e.g.*, a new and nonobvious microscope or screening assay can be used for learning about products or processes does not lessen the fact that such "tools" have legal utility. "Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have clear,

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[4] It is standard practice to screen populations of nucleic acids with EST sequences, often attached to a microarray, without characterizing each and every target mRNA. Knowing that the gene corresponding to the claimed nucleic acid molecules is expressed under certain conditions or in certain tissues or at certain levels is in itself useful. For example, such information is useful to detect expression changes in traits of interest, *e.g.*, tocopherol production and quality in a plant. Contrary to the Examiner's assertions, this use is not using the claimed nucleic acid molecules to identify a " 'real world' context or use." *See* Office Action mailed November 21, 2000, at page 6. It is a **use** of the claimed nucleic acid molecules in a real world context.

[5] One can use the claimed nucleic acid molecules to determine location of a corresponding DNA sequence on a physical map or genetic map location without knowing anything beyond the claimed sequence. The use of molecular markers is a practical activity in the development of nutritionally enhanced or agriculturally enhanced crops. Such markers are useful in, for example, genetic mapping or linkage analysis, marker-assisted breeding, physical genome mapping, transgenic crop production, crop monitoring diagnostics, and gene identification and isolation. As more markers are identified, genetic maps will become more detailed and it will be easier for plant breeders to breed for particular traits.

specific and unquestionable utility (*e.g.*, they are useful in analyzing compounds)." MPEP § 2107 at page 2100-33.

Use of the claimed nucleic acid molecules to detect the presence or absence of polymorphisms is no more legally insufficient than using a gas chromatograph to analyze the chemical composition of a gas – such use determines information about the gas, not the gas chromatograph. Even if the gas chromatograph detects the absence of a particular chemical element in the gas, that finding does not obviate the utility of the gas chromatograph itself. Information has been obtained about the gas.[6] Likewise, the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usefully demonstrates that the two (or more) populations being compared share a common genetic heritage.

Moreover, the use of the claimed nucleic acid molecules to identify the presence or absence of a polymorphism has particular relevance to the manipulation and expression of enzymes in the tocopherol pathway and in the production of tocopherol content in a plant. Applicants have disclosed that nucleic acid molecules of the present invention comprise sequences that encode enzymes of the tocopherol pathway or fragments thereof. *See*, for example, specification at page 62, lines 13-16 and Table A. The specification also discloses that the instant nucleic acids can be used for cosuppression (*e.g.*, page 50, lines 5-13) or antisense suppression (*e.g.*, page 130, line 4 to page 131, line 9), and are useful in altering the levels of enzymes of the tocopherol synthesis pathway. As such, the use of the claimed nucleic acid molecules in the isolation of chromosomes or determining the genotype of an individual plant strain

[6] For example, gas sampled from crude oil may be analyzed by gas chromatography for the presence or absence of chlorine, which is toxic to catalysts used in gasoline refining even in very low concentrations. The absence of a peak at the molecular weight of chlorine indicates the absence of chlorine in the sample being tested, thereby providing useful information (no chlorine is present, therefore the catalyst will not be destroyed) to the refinery manager. *See, e.g.*, U.S. Patent No. 6,133,740 entitled "Chlorine Specific Gas Chromatographic Detector."

clearly has an identifiable benefit. Applicants submit that the use of the claimed sequences in this manner is analogous to the use of labeled monoclonal antibodies for the isolation of cells in flow sorting in the first instance, and phenotypic/genotypic analysis in the second instance (*see, for example,* Wang *et al., Nuc. Acid Res.* 20(8):1897-901 (1992)). Both flow sorting and genotypic analysis ultimately have "real world" value at least on the breeding and selection of plants, although other utilities can be envisioned.

The claimed nucleic acid molecules have been asserted to work for a specific, *i.e.*, not vague or unknown benefit, to identify the presence or absence of a polymorphism. This benefit is immediately realized directly from the use of the claimed nucleic acids, not from the use of other molecules. Such a proven use that provides an acknowledged known benefit to the public satisfies the utility requirement of 35 U.S.C. § 101.

(b) Probes for Other Molecules or Source for Primers

Other uses for the claimed nucleic acid molecules are as probes for other molecules or as a source of primers. The specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms such as alfalfa, *Arabidopsis*, barley, *Brassica*, cotton, sunflower, *Phaseolus*, etc.[7] Specification at page 82, lines 3-18. The Examiner has not provided any evidence that would reasonably suggest that this cannot be done, and thus has not met the burden of proof required to establish a utility rejection. *See In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995). *Accord In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975); *In re Langer*, 503 F.2d 1380, 1391, 183 U.S.P.Q. 288, 297 (C.C.P.A. 1974).

[7] Furthermore, one skilled in the art of hybridization and amplification understands how to design and utilize probes and primers to target a sequence of interest, and therefore it is not necessary for Applicants to provide a laundry list of each and every nucleic acid molecule that can be identified using the claimed nucleic acid molecules.

Furthermore, Applicants assert that nucleic acid molecules of the present invention comprise sequences that encode enzymes of the tocopherol pathway or fragments thereof. *See*, for example, specification at page 62, lines 13-16 and Table A. Modulation of tocopherol content (including vitamin E) of plant tissues and changes in the levels of the enzymes in the tocopherol pathway can alter both the tocopherol content as well as the compositional quality of the vitamin E family members produced (*see, e.g.,* specification at page 2, lines 4-8). Thus, the use of the claimed nucleic acid molecules as probes or a source of primers have particular relevance to the identification of nucleic acid molecules comprising nucleic acid sequences encoding enzymes in this pathway.

The Examiner argues that the claimed nucleic acid molecules lack utility apparently because one would allegedly not be able to recognize an appropriate ATG codon or ORF for the claimed nucleic acid molecules. *See* Final Office Action at page 3. One of ordinary skill on the art would clearly be able to ascertain these elements based on Applicants' disclosure (*see, e.g.,* specification at page 171, lines 4-10) and tools available to practitioners in the art, *e.g.,* BLASTX. Moreover, the specification discloses that the nucleic acid molecules of the present invention encode tocopherol synthesis pathway enzymes or fragments thereof. Therefore, a complete ORF or start codon is not necessary for every claimed nucleic acid molecule. Furthermore, a complete ORF is not necessary to use the claimed nucleic acid molecules for the disclosed utilities, *i.e.,* as probes, to detect the presence or absence of polymorphisms, and in expression studies, all of which the Examiner acknowledges have been asserted in the specification.

In addition, for these reasons, the Examiner's assertion that homology "alone is not evidence that a particular protein is indeed encoded by a recited nucleic acid sequence" is irrelevant. Final Office Action at page 3. The Examiner has previously provided references supporting only the general controversy in the art regarding homology, but has not provided any support for the proposition that the claimed nucleic acid molecules would not work for the recited utilities; or that one skilled in the art would

doubt that the claimed nucleic acid molecules would work for the utilities disclosed in the present specification. A broad assertion of "unpredictability" in the art is not sufficient to reject the claimed invention for lack of utility.

Another illustrative example of a molecule that can be isolated using a claimed nucleic acid molecule is the promoter of the gene corresponding to that claimed nucleic acid molecule. Applicants have specifically disclosed that one use of the claimed nucleic acid molecules is to initiate a chromosome walk. Specification at page 83, line 14 through page 84, line 3. The Examiner denigrates that utility by asserting that "use as a marker is a generic use, and is not specific to any of the claimed inventions." Final Office Action at pages 2-3. In short, the Examiner suggests that the asserted utilities are legally insufficient simply because other molecules can be used for the same purpose, *i.e.*, chromosome walks. That position is wrong as a matter of law – there is no requirement of exclusive utility in the patent law. *See Carl Zeiss Stiftung v. Renishaw PLC*, 945 F.2d 1173, 1180, 20 U.S.P.Q.2d 1094, 1100 (Fed. Cir. 1991) ("An invention need not be the best or the only way to accomplish a certain result..."). Such an argument would imply that a new golf club has no legal utility because other golf clubs can be used for the same purpose, *i.e.*, hitting golf balls. That position must be rejected as it requires reading "into the patent laws limitations and conditions which the legislature has not expressed," a practice condemned by the Supreme Court. *See Diamond v. Chakrabarty*, 447 U.S. 303, 308, 206 U.S.P.Q. 193, 196 (1980), *quoting United States v. Dubilier Condenser Corp.*, 289 U.S. 178, 199, 17 U.S.P.Q. 154, 162 (1933).

Moreover, it is factually incorrect that this use is not "specific" to the claimed nucleic acid molecules. The claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate a promoter in, for example, maize or soybean that is associated with the tocopherol synthesis pathway. A random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter. Furthermore, even if a random nucleic acid molecule provided a <u>better</u>

starting point than the claimed nucleic acid molecules, it would not obviate the utility of the claimed nucleic acid molecules. An invention may be "less effective than existing devices but nevertheless meet the statutory criteria for patentability." *Custom Accessories, Inc. v. Jeffrey-Allan Indus.*, 807 F.2d 955, 960 n.12, 1 U.S.P.Q.2d 1196, 1199 n.12 (Fed. Cir. 1986).

The Examiner has failed to provide evidence, or even to suggest a reason for believing that the claimed nucleic acid molecules could not be so used. Accordingly, the assertion of this utility as a probe for other molecules or as a source of primers satisfies the requirements of 35 U.S.C. § 101. *See In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995).

(2) The Claimed Nucleic Acid Molecules Provide Practical, Real World Benefits, *i.e.*, They Have Substantial Utility

The Final Action also appears to assert that the disclosed uses are legally insufficient because they are not "substantial" utilities. Final Action at pages 2-4. The touchstone of "substantial" utility is "real world" or "practical utility." *See, e.g., Fujikawa v. Wattanasin*, 93 F.3d 1559, 1563, 39 U.S.P.Q.2d 1895, 1899 (Fed. Cir. 1996). " 'Practical utility' is a shorthand way of attributing 'real world' value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public." *Nelson v. Bowler*, 626 F.2d 853, 856, 857, 206 U.S.P.Q. 881, 883 (C.C.P.A. 1980) ("tests evidencing pharmacological activity may manifest a practical utility even though they may not establish a specific therapeutic use").[8]

There can be no question that one skilled in the art can use the claimed nucleic acid molecules in a manner which provides an immediate benefit to the public, for

[8] *Accord Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 U.S.P.Q. 739, 747-48 (Fed. Cir. 1985); *Rey-Bellet v. Engelhardt*, 493 F.2d 1380, 1383, 181 U.S.P.Q. 453, 454 (C.C.P.A. 1974).

example to detect the presence or absence of polymorphisms. The detection of polymorphisms provides an immediate benefit to the public because, *e.g.*, it enables a plant breeder to determine the distribution of parental genetic material in the progeny of a cross. This information about a plant's genetic profile, like the information about a compound's pharmacological profile in *Nelson*, provides an immediate benefit and thus a practical utility to the public.

Quite apart from the detection of polymorphisms, there is also no question that the public has recognized the benefits provided by the claimed subject matter, and has attributed "real world" value to such nucleic acid molecules. The utility of ESTs is not merely an academic issue; the real world value of ESTs is self-evident from the growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs. Like fermentation processes involving bacteria, ESTs and nucleic acid molecules with EST sequences are "industrial product[s] used in an industrial process – a useful or technical art if there ever was one." *In re Bergy*, 563 F.2d 1031, 1038, 195 U.S.P.Q. 344, 350 (C.C.P.A. 1977).

The market participants for EST products are primarily sophisticated corporations and highly knowledgeable scientists who are unlikely to pay for useless inventions. *Cf. Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 960, 220 U.S.P.Q. 592, 599 (Fed. Cir. 1983) ("People rarely, if ever, appropriate useless inventions"). Quite simply, the commercial value of ESTs is proof of their real world value and of the benefits they provide to the public. This evidence cannot be ignored. The patent system was created to serve and foster growth and development in the industrial arts. If the industries themselves recognize and appreciate the value of an invention, it is not for the Patent Office to say that they are mistaken.

(3) The Disclosed Utilities Are Credible to One of Skill in the Art

An assertion of utility must be accepted by the Examiner unless it would not be considered "credible" by a person of ordinary skill in the art. MPEP § 2107 at 2100-29. Cases in which utility was found not to be credible are rare, and usually involve "hare-brained" utilities.[9] A challenge to the credibility of a utility is essentially a challenge directed to operability, and such a challenge must be supported by a clear statement of "factual reasons which would lead one skilled in the art to question the objective truth of the statement of operability." *In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975); *see In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995); MPEP § 2107 at 2100-41.

Applicants have explicitly identified specific and substantial utilities, not only in the specification, but in Applicants' Response dated March 19, 2001, at pages 6-7 and in Applicants' Response dated January 17, 2002, at pages 6-7. "To violate [35 U.S.C.] 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 U.S.P.Q.2d 1401, 1412 (Fed. Cir. 1992). To date, the Examiner has provided no evidence that the claimed nucleic acid molecules will not work for the disclosed utilities. Unless and until the Examiner can prove that the claimed invention is wholly inoperative, the rejection must be withdrawn.

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[9] Examples of incredible utilities are given in MPEP § 2107 at page 2100-34, and include:

> an invention asserted to change the taste of food using a magnetic field (*Fregeau v. Mossinghoff*, 776 F.2d 1034, 227 U.S.P.Q. 848 (Fed. Cir. 1985)), a perpetual motion machine (*Newman v. Quigg*, 877 F.2d 1575, 11 U.S.P.Q. 1340 (Fed. Cir. 1989)), a flying machine operating on "flapping or flutter function" (*In re Houghton*, 433 F.2d 820, 167 U.S.P.Q. 687 (C.C.P.A. 1970)), a method for increasing the energy output of fossil fuels upon combustion through exposure to a magnetic field (*In re Ruskin*, 354 F.2d 395, 148 U.S.P.Q. 221 (C.C.P.A. 1966)), uncharacterized compositions for curing a wide array of cancers (*In re Citron*, 325 F.2d 248, 139 U.S.P.Q. 516 (C.C.P.A. 1963)), a method of controlling the aging process (*In re Eltgroth*, 419 F.2d 918, 164 U.S.P.Q. 221 (C.C.P.A. 1970)), and a method of restoring hair growth (*In re Ferens*, 417 F.2d 1072, 163 U.S.P.Q. 609 (C.C.P.A. 1969)).

In view of the above, Applicants contend that the claimed nucleic acid molecules are supported by credible, specific, and substantial utilities disclosed in the specification. Moreover, the Examiner has failed to raise any credible evidence challenging the presently asserted utilities. Consequently, the rejection of claims 10-18, 20-22 and 24-25 under 35 U.S.C. §101 is improper and should be reversed.

C. The Claimed Nucleic Acids Are Enabled by the Specification

The enablement of the claimed nucleic acid molecules has been challenged. Claims 10-18, 20-22 and 25 were rejected as not enabled by the specification, because the claimed nucleic acid molecules allegedly lack utility and therefore cannot be enabled. Final Action at page 4. This rejection is erroneous and has been overcome by the arguments stated above regarding utility because it is well-established law that "the enablement requirement is met if the description enables any mode of making and using the invention." *Johns Hopkins University v. CellPro*, 152 F.3d 1342, 1361, 47 U.S.P.Q.2d 1705, 1719 (Fed. Cir. 1998) (emphasis added), *quoting Engel Indus. v. Lockformer Co.*, 946 F.2d 1528, 1533, 20 U.S.P.Q.2d 1300, 1304 (Fed. Cir. 1991). Unless and until the Examiner comes forth with evidence to rebut the objective truth of the utilities disclosed in the specification, this enablement rejection must be withdrawn as improper. *See In re Wright*, 999 F.2d 1557, 1561-62, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993); *Ex parte Lemak*, 210 U.S.P.Q. 306, 307 (Bd. App. 1981) ("pure conjecture" does not substantiate rejection for lack of enablement).

D. The Specification Provides an Adequate Written Description of the Claimed Invention

Despite the Examiner's admission that the "claimed nucleic acid sequences/structures are described by the specification" (Final Action at page 4), the adequacy of the written description of claims 10-18 and 20-22 has been challenged by the Examiner because the claimed subject matter was allegedly "not described in the

specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." *Id.* The basis for the Examiner's challenge is that the claims recite open claim language (comprising) and thus "encompass sequences, comprising introns, non-coding regions and regions which do not hybridize to the claimed sequences, but which may still meet the claimed limitations..." Final Action at page 5. The Examiner alleges that the specification provides insufficient written description to support the genus encompassed by the claim. This is not a proper basis for a written description rejection of a "comprising" claim. If it was, every "comprising" claim ever written would be invalid for failing to describe every nuance of the claimed invention. Furthermore, the specification demonstrates to one skilled in the art that Applicants were in possession of the claimed genera of nucleic acid molecules.

(1) The Specification Reflects Applicants' Possession of the Claimed Invention

The purpose of the written description requirement is to ensure that the inventors had possession of the claimed subject matter, *i.e.*, to ensure that the inventors actually invented what is claimed. *Gentry Gallery Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *Lockwood v. American Airlines*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997); *In re Alton*, 76 F.3d 1168, 1172, 37 U.S.P.Q.2d 1578, 1581 (Fed. Cir. 1996). If a person of ordinary skill in the art would, after reading the specification, understand that the inventors had possession of the claimed invention, even if every nuance of the invention was not expressly described, then the written description requirement has been met. *In re Alton*, 76 F.3d at 1175, 37 U.S.P.Q.2d at 1584. After reading the present specification, a person of ordinary skill in the art would understand that Applicants had possession of nucleic acid molecules comprising SEQ ID NOs: 1, 100, 147, 153, 158, 161, 180, 184, 199, or 232, complements

thereof, and molecules which hybridize to the claimed nucleic acid sequences under the conditions specified, and therefore, the claimed invention.

Applicants have provided the nucleic acid sequences required by the claims, *i.e.*, SEQ ID NO: 1, 100, 147, 153, 158, 161, 180, 184, 199, and 232, as well as, for example, vectors comprising the nucleic acid sequence (*see, e.g.*, specification at page 111, line 6 through page 119, line 12 and at page 132, line 16 through page 138, line 4), hybridization conditions which may be used with the nucleic acid molecules of the present invention (*see, e.g.*, specification at page 60, line 16 through page 61, line 10), and binary artificial chromosomes (BIBACs) and other systems that may be used to introduce the claimed nucleic acid molecules into a host cell (*see, e.g.*, specification at page 119, lines 13-20). The fact that the claims at issue are intended to cover molecules that include the recited sequence joined with additional sequences does not mean that Applicants were any less in possession of the claimed nucleic acid molecules.[10] It is well-established that use of the transitional term "comprising" leaves the claims "open for the inclusion of unspecified ingredients even in major amounts." *Ex parte Davis*, 80 U.S.P.Q. 448, 450 (B.P.A.I. 1948). *Accord PPG Indus. v. Guardian Indus.*, 156 F.3d 1351, 1354, 48 U.S.P.Q.2d 1351, 1353-54 (Fed. Cir. 1998); *Moleculon Research Corp. v. CBS*, 793 F.2d 1261, 1271, 229 U.S.P.Q. 805, 812 (Fed. Cir. 1986).

Applicants have provided in the present disclosure not only the nucleotide sequences required by the claims (i.e. SEQ ID NOs: 1, 100, 147, 153, 158, 161, 180, 184, 199, and 232), but also several variations including and directed to the claimed nucleic acid molecules. For example, the present specification describes vectors comprising the claimed nucleic acid molecules (specification at page 111, line 6 through page 119, line

[10] If the Examiner is arguing that no possession is shown because the precise claim language is not used in the specification, then she goes beyond what is required by the law. It is well-settled that the description of a claimed invention need not be *in ipsis verbis*. *Gentry Gallery v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *In re Alton*, 76 F.3d 1168, 1175, 37 U.S.P.Q.2d 1578, 1583 (Fed. Cir. 1996); *Martin v. Johnson*, 454 F.2d 746, 751, 172 U.S.P.Q. 391, 395 (C.C.P.A. 1972).

12, and at page 132, line 16 through page 138, line 4), and describes how to make the nucleotide sequences and libraries from which they were originally purified. *See, e.g.*, specification at page 12, line 7 through page 14, line 10 and Examples 1-3.). Furthermore, the addition of extra nucleotides or detectable labels to the disclosed nucleotide sequences (SEQ ID NOs: 1, 100, 147, 153, 158, 161, 180, 184, 199, and 232) is readily envisioned by one of ordinary skill in the art upon reading the present specification,[11] for example, at page 76, line 21 through page 77, line 8 (describing fusion peptide molecules encoded by the claimed nucleic acid molecules), page 69 line 20 through page 72, line 2 (describing the identification of SNPs), page 105, line 15 through page 107, line 7 (describing site-directed mutagenesis) and page 163, line 22 through page 164, line 6 (citing references describing the construction, manipulation and isolation of nucleic acid macromolecules).

Moreover, the court determined, in *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1321, 63 U.S.P.Q.2d 1609, 1610 (Fed. Cir. 2002), that the written description inquiry is a factual one determined on a case-by-case basis and that, in a given disclosure, "it may well be that various subsequences, mutations, and mixtures of those sequences are also described to one of skill in the art." *Enzo*, 296 F.3d at 1326-1327, 63 U.S.P.Q.2d at 1615. Furthermore, it is well established that claims "may be broader than the specific embodiment disclosed in a specification. *Ralston-Purina Co. v. Far-Mor-Co*, 772 F.2d 1570, 1575, 227 U.S.P.Q. 177, 179 (Fed. Cir. 1985) (*quoting In re Rasmussen*, 650 F.2d 1212, 1215, 211 U.S.P.Q. 323, 326 (C.C.P.A. 1981).

[11] It is established patent jurisprudence that Applicants need not teach "conventional and well-known genetic engineering techniques." *E.g., Ajinomoto Co. v. Archer-Daniels-Midland Co.*, 228 F.3d 1338, 1345, 56 U.S.P.Q.2d 1332, 1337 (Fed. Cir. 2000).

(2) Applicants Have Described the Claimed Invention

The Examiner asserts that because Applicants have not disclosed any "sequences/structures, such as corresponding sequences from other species derivatives, allelic variants, splice variants, and so forth", Applicants have not adequately disclosed the claimed genera of nucleic acid molecules. Office Action mailed April 10, 2002, at page 8. The Examiner appears to assert that each nucleic acid molecule within the claimed genera must be described by its complete structure. These assertions are totally unfounded. The Federal Circuit has elucidated a test for written description wherein a genus of nucleic acids may be described by a structural feature that distinguishes members of the claimed genus from non-members of the claimed genus. *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568-69, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997). Applicants have satisfied that test for written description.

In particular, Applicants have disclosed common structural features, for example, the nucleotide sequences of SEQ ID NOs: 1, 100, 147, 153, 158, 161, 180, 184, 199 and 232. The respective common structural feature (the nucleotide sequences of SEQ ID NOs: 1, 100, 147, 153, 158, 161, 180, 184, 199 and 232) is shared by <u>every</u> nucleic acid molecule in the claimed genera, and it distinguishes the members of the claimed genera from non-members. For example, if a nucleic acid molecule such as an mRNA contains the nucleotide sequence of SEQ ID NO: 1, then it is a member of the claimed genus of nucleic acid molecules comprising a nucleic acid sequence of SEQ ID NO: 1.[12] If a nucleic acid molecule does not contain SEQ ID NO: 1, then it is not a member of that claimed genus. The presence of other nucleotides at either end of the recited sequence will not interfere with the recognition of a claimed nucleic acid molecule as such – it either contains the nucleotides of SEQ ID NO: 1 or it does not. One skilled in the art,

[12] The same argument applies with equal force to every genus of the claimed nucleic acid molecules. For example, if a nucleic acid molecule such as an mRNA contains the nucleotide sequence of SEQ ID NO: 100, then it is a member of the claimed genus of nucleic acid molecules comprising a nucleic acid sequence of SEQ ID NO: 100. *See, e.g.*, claim 13.

after reading the present specification, would clearly know if a nucleic acid molecule contains one of the recited nucleotide sequences. Thus, claims 10-18 and 20-24 are supported by an adequate written description pursuant to the requirements of 35 U.S.C. § 112, and the rejection should be reversed.

CONCLUSION

In view of the foregoing, it is respectfully requested that the Board of Patent Appeals and Interferences reverse the Rejections and that the subject application be allowed forthwith.

Respectfully submitted,

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APPENDIX A

10. An isolated nucleic acid molecule comprising a sequence that hybridizes under conditions of 2.0 X sodium chloride/sodium citrate (SSC) at about 65°C to a nucleic acid molecule having a sequence selected from the group consisting of SEQ ID NOs: 100, 147, 153, 180, 199, 232 and complements thereof.

11. The isolated nucleic acid molecule, according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence selected from the group consisting of SEQ ID NO: 100, SEQ ID NO: 147, SEQ ID NO: 153, SEQ ID NO: 180, SEQ ID NO: 199, and SEQ ID NO: 232 and complements thereof.

12. An isolated nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1 or complement thereof.

13. The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 100 or complement thereof.

14. The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 147 or complement thereof.

15. The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 153 or complement thereof.

16. An isolated nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 158 or complement thereof.

17. An isolated nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 161 or complement thereof.

18. The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 180 or complement thereof.

20. The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 199 or complement therof.

21. The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 232 or complement thereof.

22. An isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 100, SEQ ID NO: 147, SEQ ID NO: 153, SEQ ID NO: 158, SEQ ID NO: 161, SEQ ID NO: 180, SEQ ID NO: 184, SEQ ID NO: 199, SEQ ID NO: 232, and complements thereof.

25. An isolated nucleic acid molecule consisting of a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 100, SEQ ID NO: 147, SEQ ID NO: 153, SEQ ID NO: 158, SEQ ID NO: 161, SEQ ID NO: 180, SEQ ID NO: 184, SEQ ID NO: 199, SEQ ID NO: 232, and complements thereof.